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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/669,833	09/26/2000	Linda S. Mansfield	MSU 4.1-528	2531

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EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Copy

Office Action Summary	Application No.	Applicant(s)	
	09/669,833	Mansfield et al	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

✓4)☒ Claim(s) 29-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

✓6)☒ Claim(s) 29-35 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's preliminary amendment filed on 9/26/01 (Paper # 3) is acknowledged Claims 1-28 and 36-50 have been canceled. Claims 29-35 are pending in the application.

Priority

2. This application is a divisional application of co-pending application 09/513,086, which claims priority to Provisional Application 60/152,193 on 9/2/1999.

Information Disclosure Statement

3. The information disclosure statement filed 9/26/01 (Paper # 2) is acknowledged and a signed copy is attached to this Office Action.

Specification - Informalities

4. Applicant is advised to delete the lines 5-10 on page 1 of specification since the invention is not sponsored by Federal agency. The specification page 11, line 3 states that "the present invention will become increasingly apparent by reference to the following embodiments and drawings". However, no drawings have been filed with the application. Therefore, applicant is advised to correct the specification. Applicant is advised to correct any other errors that applicant might come across in the application.

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

Since it is not clear from the claims whether applicant is claiming a method to produce antibodies to a fusion peptide comprising at least one epitope encoding a 16(±4) kD antigen and 30(±4) kD antigen of S.neurona or a method to produce antibody comprising providing parasite proteins 16(±4) kD antigen and 30(±4) kD together, Examiner is interpreting this method for producing an antibody comprising providing a microorganism in a culture containing a DNA encoding **a fusion polypeptide** (i.e., recombinant fusion polypeptide)comprising at least one epitope encoding a 16(±4) kD antigen and 30(±4) kD antigen of S.neurona.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

The claims encompass a method for producing antibody comprising providing a microorganism in a culture containing a DNA encoding a fusion polypeptide comprising at least one epitope encoding a 16(±4) kD antigen and /or 30(±4) kD antigen of S.neurona. Review of the present specification, the art of record, and a search of the sequence databases for polypeptide and polynucleotide sequences 16(±4) kD antigen and the 30(±4) kD antigen indicate that these sequences have not been identified nor described. Presently, in order to

practice the invention as claimed the artisan must first obtain the polypeptide and/or polynucleotide sequences of the 16(±4) kD antigen and the 30(±4) kD antigen. The specification describes general methods of cloning cDNA sequences from expression libraries; however, the sequences obtained by this method are not disclosed. The specification fails to provide any detail to any of the sequences of the 16(±4) kD antigen or the 30(±4) kD antigen. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicant's effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, the claimed embodiments of the polypeptide and polynucleotide sequences needed to make and use the invention as claimed lack a written description. The specification fails to describe any polynucleotides or polypeptides encompassed in the claims with particularity to indicate that Applicants had possession of the claimed invention. The written description of a claim is evaluated on the basis of the claimed invention as a whole. Case law established that the requirement for written description relates to the subject matter defined by the claims. *In re Wright*, 9 USPQ2d 1649 (Fed. Cir. 1989). To this end, while antibodies exist which recognize a 16(±4) kD antigen or a 30(±4) kD antigen, no specific sequence which is recognized by these antibodies is disclosed. The claimed invention is directed to a fusion protein comprising providing a microorganism in a culture containing a DNA encoding one epitope 16(±4) kD antigen and /or 30(±4) kD antigen of S.neurona and the specification fails to demonstrate possession of the invention by actual reduction to practice. The skilled artisan cannot envision the detailed structure of the claimed recombinant protein

encoded by DNA, nor the materials necessary to practice the methods steps necessary to carry out the claimed methods of generating recombinant protein which would serve as an antigen/vaccine, and thus, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Case law has established that one cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art **as of Applicants effective filing date**. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

6. Claims 29-35 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention since there is lack of written description for the claimed invention.

Claim Rejections - 35 USC 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 29-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 30 are rejected as being vague and indefinite for the recitation of "or ". Applicant is claiming a method to produce an antibody to a fusion polypeptide comprising at least one epitope of a 16KD (+/- 4) antigen and 30 KD (+/- 4) antigen. Therefore, the recitation of "or" is vague.

Claims 29 and 30 are rejected as being vague and indefinite because it is not clear that the fusion polypeptide comprises one epitope of a 16KD (+/- 4) antigen and one epitope of 30 KD (+/- 4) antigen or one epitope of 16KD (+/- 4) and 30 KD (+/- 4) antigen.

Claims 29-30 are rejected as being vague and indefinite for the recitation of "polypeptide that facilitates isolation of the fusion polypeptide". How can a polypeptide facilitate isolation of fusion peptide.

Claims 29-30 are rejected as being vague and indefinite for the recitation of "from the polypeptide". It is not clear how to produce an antibody from a polypeptide?

Claim 31 should read as "wherein the fusion polypeptide is isolated by affinity chromatography".

Claim 32 is rejected as being vague and indefinite for the recitation of "polypeptide is all or a portion of protein A". How can a fusion polypeptide contain all protein A? Does applicant mean to recite that a fusion polypeptide contains one epitope of a 16KD (+/- 4) antigen and one epitope of 30 KD (+/- 4) antigen and protein A?

Claims 33, 34 and 35 are rejected as being vague for the recitation of "polypeptide is polyhistidine, glutathione and maltose binding protein respectively". Does this mean fusion polypeptide further comprises polyhistidine, glutathione and maltose binding protein respectively?

Claim 29 is rejected as being vague and indefinite for the recitation of "(±4)." It is not clear whether this is intended to be a limitation of the claims. Applicant is advised to remove the parenthesis.

9. Claims 29-36 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, See MPEP. § 2172.01.

Claims 29-30 are drawn to a method for producing either an antibody or a monoclonal antibody. However, the claims are incomplete because they do not recite any active step for producing antibodies. There is no step which indicates that the polypeptide is contacted with the animal or something else. Applicant is advised to amend the claim to recite method steps for the production of either polyclonal or monoclonal antibodies.

10. Further, it is unclear how an additional polypeptide that facilitates the fusion polypeptide is related to the 30(±4) KD antigen and the16 (±4) KD antigen since this now can read on a second DNA encoding said polypeptide, which facilitates isolation of fusion peptide. It appears that 30(±4) KD antigen and at least one epitope of a 16(±4) KD antigen are not physically linked to the fusion protein at all. In addition, the claim recites at least 'one epitope of a 16(±4) kD antigen **or** 30(±4) kD antigen' makes it unclear if the microorganism in a culture containing a DNA encodes a fusion protein with at least one antigen of a 16(±4) or a microorganism in a culture containing a DNA encodes an antigen of a 30(±4) which would then would encompass culturing and isolating an endogenous form of the 30(±4) protein.

Claim Rejections - 35 USC 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a

whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liang et al 1997 (Analytical Biochemistry; 250 (1) 61-5) or Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) or Grandstrom et al 1993 (J.Vet. Diagn 5: 88-90) in view of Harlow and Lane 1988 (Antibodies; Cold Spring Harbor).

Claims are directed to a method for producing an antibody containing a DNA encoding a fusion polypeptide comprising at least one epitope of a 16KD (+/- 4) antigen **or** 30 KD (+/- 4) antigen.

Since the claims fail to recite or characterize either the DNA or the protein with either sequence details such as how many amino acids are present in these polypeptides or Sequence identification numbers, Examiner is interpreting a DNA encoding a fusion protein broadly and applying the art against S.neurona merozoites because the parasite 's DNA encodes both .e., 16 +/- 4 antigen and 30KD antigen.

Liang et al 1997 (see page 65, right column, last paragraph) or Liang et al 1998 (see figure 1 and page 1835, right column, first paragraph, figure 3 B) disclose a purified 19KD (i.e., 16 +/- 4 antigen) antigen or 30KD antigen from S.neurona merozoites. Grandstrom et al 1993

disclose (see abstract) about 8 surface antigens including 24KD (i.e., 30 KD +/- 4) and 13KD (i.e., 16KD +/- 4).

Liang et al 1997 (see page 65, right column, last paragraph) or Liang et al 1998 (see figure 1 and page 1835, right column, first paragraph, figure 3 B), teach purified 19KD (i.e., 16 +/- 4 antigen) antigen or 30KD antigen from S.neurona merozoites are involved in humoral immunity. Grandstrom et al 1993 teaches about 8 surface antigens including 24KD (i.e., 30 KD +/- 4) or 13KD (i.e., 16KD +/- 4), which are recognized by immune serum from horses. However, the Prior art does not teach a method of producing antibodies against these proteins.

It is well known and routine in the art of immunology method of producing monoclonal antibodies and polyclonal antibodies, which bind to specific antigens or antigen epitopes. (Harlow and Lane 1988). However, the prior art does not teach specifically producing monoclonal antibodies and polyclonal antibodies to 16KD (+/- 4) antigen or 30 KD (+/- 4) antigen from S.neurona merozoites.

Liang et al 1997 or 1998 teach the importance of surface proteins Sn14 and Sn 16 of S.neurona merozoites, which may be useful in vaccine preparation, and merozoites, which are potential targets for specific antibodies (see abstract). Further, the prior art suggests S.neurona infection of the horses induce antibodies to Sn14 and Sn 16 indicating that these proteins are strong immunogens and specific antibodies may lyse the merozoites via complement, inhibit their infection (see Discussion). Grandstrom et al also teach about the importance surface proteins including 24 KD, 13KD etc. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to raise monoclonal or polyclonal antibodies to different potent surface antigens such as 16kD or 30kD which could be used in diagnostics or to treat infection with a reasonable expectation of success because it would help to treat or cure or diagnose the infection in horses as suggested by Liang et al et al. An artisan

of ordinary skill would have been motivated in applying the art disclosed by the prior art Liang et al 1997/98 or Grandstrom et al to Harlow and Lane to prepare antibodies to surface proteins because Liang et al suggests that protective humoral immunity to S.neurona infection is important. The claimed invention is prima facie obvious over Liang et al 1997 or Liang et al 98 or Grandstrom et al each in view of Harlow and Lane 1986 (chapter 6) absent any convincing evidence to the contrary.

Status of Claims

13. Claims 29-35 are rejected

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

12/15/01